

LEWIS – EXHIBIT 1

Curriculum Vitae: Dr Richard James Lewis

Position: Associate Professor and Group Leader

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The University of Queensland
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Academic Qualifications:

BSc (James Cook University) 1977
PhD (The University of Queensland) 1985

Date of Birth: 17 July 1957, Brisbane

Membership of Professional Societies:

International Society on Toxinology
Australian Society for Biochemistry and Molecular Biology Inc.
International Association for the Study of Pain
American Society for Biochemistry and Molecular Biology

Research History:

1981 - 1984 Research Assistant, University of Queensland
1985 Visiting scientist at the Max-Planck Institute, Dortmund, FRG
1986 - 1992 Fisheries Biologist and Senior Fisheries Biologist, QDPI
1992 - 1998 Principal Fisheries Biologist, QDPI
1998 - 2000 Principal Scientist, QDPI
1996 - 2000 Principal Investigator, Institute for Molecular Bioscience (formerly 3D Centre)
1996 - 1998 Adjunct Senior Lecturer, Department of Physiology and Pharmacology, The University of Queensland
1999 - present Adjunct Reader, Department of Physiology and Pharmacology, The University of Queensland
2000 - present Principal Research Fellow, IMB, The University of Queensland
2000 - present Research Director, Pharmacology, Xenome Ltd

Professional Experience:

- Conducted original, multidisciplinary research on marine toxins (> 25 years experience);
- lead large, multidisciplinary research teams;
- contribute broadly to the pharmacology of toxins, especially those targeting transporters GPCRs, and sodium and calcium channels involved in pain pathways;
- attracted external funding and prepare research reports for granting bodies and industry;
- foundation Director of Pharmacology, Xenome, a UQ spin-off company commercialising conotoxin research;
- consultant to AMRAD on ω -conotoxin SAR and pharmacology.

Postgraduate training:

Principal supervisor for 4 successful PhDs
Principal supervisor for 6 current PhD students
Associate supervisor for 5 PhD students

Research achievements:

- obtained over \$2,600,000 in commercial funding in the last 6 years at UQ;
- led the discovery, and inventor on a patent covering a novel ω -conotoxin therapeutic for pain which has gain TGA approval to enter clinical trials conducted by AMRAD, with rights to the royalty returns to UQ acquired by Xenome for ~ \$6 million;
- led the discovery, and inventor on two patents covering two new classes of conotoxin with novel pharmacology and commercial potential that have been acquired by Xenome and developed into novel treatment for neuropathic pain;
- determined the structure and structure activity relationships for several ciguatoxins;
- led the development of analytical methods for ciguatoxin detection and the implementation of the mannitol therapy for ciguatera in Australia;
- Inventor on seven patents.

International recognition:

- internationally recognised expert on marine toxins, especially ciguatoxins and conotoxins;
- regularly invited to present lectures and plenary lectures at international conferences, including *Gordon Conference on Mycotoxins and Phycotoxins*, the *International Conference on Harmful Algal Blooms*, and the *International Conference on Toxinology*;
- regularly invited to contribute reviews on ciguatera and conotoxins in books and journals;
- Phycotoxin Chair for the 2001 "Gordon Conference on Mycotoxins and Phycotoxins";
- member of the organising and editorial committees for the 9th *International Conference on Harmful Algal Toxins*;
- Co-chair of the Scientific Organising Committee for the 12th International society for Toxinology meeting in 2003.

Original refereed publications:

1. Cameron, A.M., Surridge, J., Stablum, W. and Lewis, R.J. (1981). A crinotoxin from the skin tubercle glands of a stonefish (*Synanceia trachynis*). *Toxicon* 19, 159-170.
2. Cameron, A.M. and Lewis, R.J. (1982). The antispasmodic action on guinea-pig ileum of a fraction obtained from the toxic skin secretion of the stonefish, *Synanceia trachynis*. *Toxicon* 20, 991-1000.
3. Pearn, J.H. Hervey, J. De Ambrosis, M. Lewis, R.J. and MacKay, R. (1982). Ciguatera and pregnancy. *Med. J. Aust.* 1, 51-58.
4. Cameron, A.M., Wong Hoy, A.W. and Lewis, R.J. (1983). The effects of two stonefish skin toxins on guinea pig atria. *Toxicon* Suppl. 3, 53-56.
5. Endean, R., Lewis, R.J., Gyr, P. and Williamson, J. (1983). Toxic material from the crab *Atergatis floridus*. *Toxicon* Suppl. 3, 11-113.
6. Lewis, R.J. and Endean, R. (1983). The occurrence of a ciguatoxin-like substance in the Spanish mackerel (*Scomberomorus commersoni*). *Toxicon* 21, 19-24.
7. Lewis, R.J. and Endean, R. (1983). Purification of ciguatoxin-like material from *Scomberomorus commersoni* and its effect on the rat phrenic nerve-diaphragm. *Toxicon* Suppl. 3, 249-252.
8. Lewis, R.J. and Endean, R. (1984). Mode of action of ciguatoxin from the Spanish mackerel, *Scomberomorus commersoni*, on the guinea pig ileum and vas deferens. *J. Pharm. Exp. Ther.*

9. Lewis, R.J. and Endean, R. (1984). Ciguatoxin from the flesh and viscera of the barracuda, *Sphyrna jello*. *Toxicon* 22, 805-810.
10. Gillespie, N., Lewis, R., Holmes, M., Burke, J. et al. (1986). Ciguatera in Australia: occurrence, clinical features, pathophysiology and management. *Med. J. Aust.* 145, 585-590.
11. Lewis, R.J. and Endean, R. (1986). Direct and indirect effects of ciguatoxin on guinea-pig atria and papillary muscles. *Naunyn Schmiedeberg's Arch Pharmacol.* 334, 313-323.
12. Lewis, R. (1988). Negative inotropic and arrhythmic effects of high doses of ciguatoxin on guinea pig atria and papillary muscles. *Toxicon* 26, 639-649.
13. Pearn, J.H., Lewis, R.J., Ruff, T., Tait, T., Quinn, J., Murtha, W., King, G., Mallet, A. and Gillespie, N.C. (1989). Ciguatera and mannitol: experience with a new treatment regimen. *Med. J. Australia* 151, 77-80.
14. Holmes, M.J., Lewis, R.J. and Gillespie, N.C. (1990). Toxicity of Australian and French Polynesian strains of *Gambierdiscus toxicus* (Dinophyceae) grown in culture: characterisation of a new type of maitotoxin. *Toxicon* 28, 1159-1172.
15. Holmes, M.J., Lewis, R.J., Poli, M.A. and Gillespie, N.C. (1991). Strain dependant production of ciguatoxin precursors (gambiertoxins) by *Gambierdiscus toxicus* (Dinophyceae) in culture. *Toxicon* 29, 761-775.
16. Lewis, R.J., Sellin, M., Poli, M.A., Norton, R.S., MacLeod, J.K. and Sheil, M.M. (1991). Purification and characterisation of ciguatoxins from moray eel (*Lycodontis javanicus*, Muraenidae). *Toxicon* 29, 1115-1127.
17. Lewis, R. J. (1992). Ciguatoxins are potent ichthyotoxins. *Toxicon* 30, 207-211.
18. Lewis, R. J. and Sellin, M. (1992). Multiple ciguatoxins in the flesh of fish. *Toxicon* 30, 915-919.
19. Lewis, R. J. (1992). Socioeconomic impacts and management of ciguatera in the Pacific. *Bull. Soc. Path. Exot.* 85, 427-434.
20. Dickey, R.W., Benscath, F.A., Granade, H.R. and Lewis, R. J. (1992). Liquid chromatographic mass spectrometric methods for the determination of marine polyether toxins. *Bull. Soc. Path. Exot.* 85, 514-515.
21. Lewis, R. J., Wong Hoy, A. W. and McGiffin, D. C. (1992). Action of ciguatoxin on human atrial trabeculae. *Toxicon* 30, 907-914.
22. Lewis, R. J. and Wong Hoy, A. W. (1993). Comparative action of three major ciguatoxins on guinea-pig atria and ilea. *Toxicon* 31, 437-446.
23. Lewis, R. J., Brereton, I. M. and Eccles, C. D. (1993) Ciguatoxin-2 is a diastereomer of ciguatoxin-3. *Toxicon* 31, 637-643.
24. Lewis, R. J., Wong Hoy, A. W. and Sellin, M. (1993) Ciguatera and mannitol: *in vivo* and *in vitro* assessment in mice. *Toxicon* 31, 1039-1050.
25. Lewis, R. J. and Ruff, T. A. (1993) Ciguatera: ecological, clinical and socioeconomic perspectives. *Critical Rev. Env. Sci. Tech.* 23, 137-156.
26. Lewis, R. J. and Sellin, M. (1993) Recovery of ciguatoxin from fish flesh. *Toxicon* 30, 915-919.
27. Lewis, R. J. and Holmes, M. J. (1993) Origin and transfer of toxins involved in ciguatera. *Comp. Biochem. Physiol.* 106C, 615-628.

28. Holmes, M. J. and Lewis, R. J. (1994) Purification and characterisation of large and small maitotoxins from cultured *Gambierdiscus toxicus*. *Natural Toxins* 2, 64-72.
29. Lewis, R.J. (1994) Immunological, biochemical and chemical features of the ciguatoxins: implications for detection of ciguateric fish. *Memoirs Qld. Mus.* 34, 541-548.
30. Lewis, R. J. (1994) Impact of a validated, cost effective screen for ciguateric fish. *Memoirs Qld. Mus.* 34, 549-554.
31. Holmes, M. J., Lewis, R. J., Sellin, M. and Street, R. (1994) The origin of ciguatera in Platypus Bay, Australia. *Memoirs Qld. Mus.* 34, 505-512.
32. Lewis, R. J. and Brereton, I. M. (1994) Short and long range inverse detected NMR of Ciguatoxin-1. *Memoirs Qld. Mus.* 34, 555-560.
33. Lewis, R. J., Holmes, M. J. and Sellin, M. (1994) Invertebrates implicated in the transfer of gambiertoxins to the benthic carnivore *Pomadourys maculatus*. *Memoirs Qld. Mus.* 34, 561-564.
34. Lewis, R. J., Sellin, M., Gillespie, N. C., Holmes, M. J., Keys, A., Street, R., Smythe, H., Thaggard, H. and Bryce, S. (1994) Ciguatera and herbivores: uptake and accumulation of ciguatoxins in *Ctenochaetus striatus* on the Great Barrier Reef. *Memoirs Qld. Mus.* 34, 565-570.
35. Lang, R. J., Vogalis, F., Holmes, M. J. and Lewis, R. J. (1994) Maitotoxin induces muscle contraction and a non-selective cationic current in single smooth muscle cells of the guinea-pig proximal colon. *Memoirs Qld. Mus.* 34, 533-540.
36. Holmes, M. J. and Lewis, R. J. (1994) The origin of ciguatera. *Memoirs Qld. Mus.* 34, 497-504.
37. Pearn, J.H. and Lewis, R.J. (1994) Ciguatera: risk perception and fish ingestion. *Memoirs Qld. Mus.* 34, 605-608.
38. Ruff, T.A. and Lewis, R.J. (1994) Clinical aspects of ciguatera; an overview. *Memoirs Qld. Mus.* 34, 609-620.
39. Lewis, R. J., Bingham, J-P., Jones, A. and Alewood, P. F. (1994) Analysis of *Conus* venoms by ionspray mass spectrometry. *Australasian Biotech.* 4, 298-300.
40. Lewis, R. J., Holmes, M. J., Alewood, P. F. and Jones, A. (1994) Ionspray mass spectrometry of ciguatoxin-1, maitotoxin-2 and -3 and related polyether toxins. *Natural Toxins* 2, 56-63.
41. Lau, C.O., Tan, C.H., Khoo, H.E., Yuen, R., Lewis, R.J., Corpuz, G.P. and Bignami, G.S. (1995) *Lyphozozymus pictor* toxin: a fluorescent structural isomer of palytoxin. *Toxicon* 33, 1373-1377.
42. Hamblin, P., McLachlan, E. M. and Lewis, R. J. (1995) The action of sub-nanomolar concentrations of ciguatoxin-1 in guinea pig sympathetic ganglia. *Naunyn Schmiedeberg's Arch. Pharmacol.* 352, 236-246.
43. Brock, J. A., Jobling, P., McLachlan, E. M. and Lewis, R. J. (1995) Electrical activity in rat tail artery during asynchronous activation of postganglionic nerve terminals by ciguatoxin-1. *Br. J. Pharmacol.* 116, 2213-2220.
44. Holmes, M. J., Lewis, R. J., Jones, A. and Wong Hoy, A.W. (1995) Cooliatoxin, the first toxin from *Coolia monotis* (Dinophyceae). *Natural Toxins* 3, 355-362.
45. Manger, R.L., Lee, S.Y., Leja, L.S., Hungerford, J.M., Hokama, Y., Dickey, R.W., Granade, H.R., Lewis, R.J., Yasumoto, T. and Wekell, M.M. (1995) Detection of sodium channel toxins: directed cytotoxicity assays of purified ciguatoxins, brevetoxins, saxitoxins, and seafood extracts. *J. Assoc. Off. Anal. Chem.* 78, 521-527.

46. Jones, A., Bingham, J-P., Gehrman, J., Bond, T., Loughnan, M., Atkins, A., Lewis, R.J. and Alewood, P.F. (1996) Isolation and characterisation of conopeptides by high-performance liquid chromatography combined with mass spectrometry and tandem mass spectrometry. *Rapid Commun. Mass Spectrom.* **10**, 138-143.
47. Lewis, R., Alewood, P., Dooley, M., Martin, J., Drinkwater, R., Craik, D and Andrews, P. (1996) Secrets of the cone shell. *Today's Life Science* **8**, 16-24.
48. Neilsen, K.J., Thomas, L., Lewis, R.J., Alewood, P.F. and Craik, D.J. (1996) A consensus structure for ω -conotoxins with different selectivities for voltage sensitive calcium channel subtypes: comparison of MVIIA, SVIB and SNX-202. *J. Mol. Biol.* **263**, 297-310.
49. Poli, M., Lewis, R.J., Dickey, R.W., Musser, S.M., Buckner, C.A. and Carpenter, L.G. (1997) Identification of Caribbean ciguatoxins as the cause of an outbreak of fish poisoning among U.S. soldiers in Haiti. *Toxicon* **35**, 733-741.
50. Lewis, R. and Jones, A. (1997) Characterisation of ciguatoxins and ciguatoxin congeners present in ciguateric fish by gradient reverse phase HPLC/mass spectrometry. *Toxicon* **35**, 159-168.
51. Vernoux, J-P. and Lewis, R.J. (1997) Isolation and characterisation of Caribbean ciguatoxins from the horse-eye jack (*Caranx latus*). *Toxicon* **35**, 889-900.
52. Fenner, P., Lewis, R. Williamson, J. and Williams, M. (1997) Ciguatera poisoning - identification of the toxins and clinical picture. *Med. J. Australia* **166**, 473-475.
53. Lucas, R.E., Lewis, R.J. and Taylor, J.M. (1997) Pacific ciguatoxin-1 associated with a large common-source outbreak of ciguatera in east Arnhem Land, Australia. *Natural Toxins* **5**, 136-140.
54. Skjærbaek, N., Nielsen, K.J., Lewis, R.J., Alewood, P.F. and Craik, D.J. (1997) Determination of the structure of conantokin-G and conantokin-T by CD and NMR spectroscopy. *J. Biol. Chem.* **272**, 2291-2299.
55. Scanlon, M.J., Naranjo, D., Thomas, L., Alewood, P.F., Lewis, R.J. and Craik, D.J. (1997) Solution structure and proposed binding mechanism of a novel potassium channel toxin κ -conotoxin PVIIA. *Structure* **5**, 1585-1597.
56. Lewis, R.J., Vernoux, J-P. and Brereton, I.M. (1998) Structure of Caribbean ciguatoxin isolated from *Caranx latus*. *J. Am. Chem. Soc.* **120**, 5914-5920.
57. Loughnan, M., Bond, T., Atkins, A., Cuevas, J., Adams, D.J., Broxton, N., Livett, B., Down, J., Jones, A., Alewood, P.F. and Lewis, R.J. (1998) α -Conotoxin Epl: a novel sulfated peptide from *Conus episcopatus* which selectively targets neuronal nicotinic acetylcholine receptors. *J. Biol. Chem.* **273**, 15667-15674.
58. Hu, S-H., Loughnan, M., Miller, R., Weeks, C.M., Blessing, R.H., Alewood, P.F., Lewis, R.J. and Martin, J.L. (1998) A novel α -conotoxin, Epl from *Conus episcopatus*: the 1.1 Å crystal structure of [Tyr¹⁵]-Epl solved by direct methods. *Biochemistry* **37**, 11425-11433.
59. Hogg, R.C., Lewis, R.J. and Adams, D.J. (1998) Ciguatoxin (CTX-1) modulates single tetrodotoxin-sensitive sodium channels in rat parasympathetic neurones. *Neuroscience Lett.* **252**, 103-106.
60. Moore, M.R., Ng, J. and Lewis, R.J. (1998) Environmental poisoning: presentation and management. *Ther. Drug Monit.* **20**: 502-509.
61. Strachan, L.C., Nicholson, G.M. and Lewis, R.J. (1999) Differential actions of ciguatoxin on sodium channel subtypes in mammalian sensory neurons. *J. Pharm. Exp. Ther.* **288**, 379-288.
62. Lewis, R.J., Jones, A., Vernoux, J-P. and Marquais, M. (1999) HPLC-tandem mass spectrometry for

the determination of sub-ppb levels of Pacific and Caribbean ciguatoxins in crude extracts of fish. *Anal Chem.* **71**, 247-250.

63. Nielsen, K.J., Skjærbæk, N., Dooley, M., Adams, D.A., Mortensen, M., Dodd, P., Craik, D.J., Alewood, P.F. and Lewis, R.J. (1999) Structure activity studies of conantokins as human NMDA receptor modulators. *J. Med. Chem.* **42**, 415-426.
64. Nielsen, K.J., Adams, D.A., Alewood, P.F., Lewis, R.J., Thomas, L., Schroeder, T. and Craik, D.J. (1999) The effect of chirality at Tyr13 on the structure-activity relationships of ω -conotoxins from *Conus magus*. *Biochemistry* **38**, 6741-6751.
65. Adams, D., Alewood, P., Craik, D., Drinkwater, R., and Lewis, R.J. (1999) Conotoxins and their potential pharmaceutical applications. *Drug Discovery Research* **46**, 219-234.
66. Hogg R.C., Miranda L.P., Craik D.J., Lewis R.J., Alewood P.F. and Adams D.J. (1999) Single amino acid substitutions in α -conotoxin PnIA shift selectivity for subtypes of the mammalian neuronal nicotinic acetylcholine receptor. *J. Biol. Chem.* **274**, 36559-36564.
67. Nielsen K.J., Adams D., Thomas L., Bond T., Alewood P.F., Craik D.J. and Lewis R.J. (1999) Structure-activity relationships of ω -conotoxins MVIIA, MVIIIC and 14 loop splice hybrids at N and P/Q-type calcium channels. *J. Mol. Biol.* **289**, 1405-1421.
68. Eriksson, L., Guy, S., Perlmutter, P. and Lewis, R. (1999) A short synthesis of the A/B ring systems of the Pacific ciguatoxins P-CTX-3C and dihydroxy-P-CTX-3C. *J. Org. Chem.* **64**, 8396-8398.
69. Nielsen, K., Schroeder, T. and Lewis, R.J. (2000) Structure-activity relationships of ω -conotoxins. *J. Mol. Recognition* **13**, 55-70.
70. Lewis R.J. (2000) Ion channel toxins and therapeutics: from cone snail venoms to ciguatera. *Ther Drug Monit.* **22**, 61-64.
71. Lehane L, Lewis R.J. (2000) Ciguatera: recent advances but the risk remains *Int J Food Microbiol.* **61**, 91-125.
72. Hill JM, Atkins AR, Loughnan ML, Jones A, Adams DA, Martin RC, Lewis RJ, Craik DJ, Alewood PF. (2000) Conotoxin TVIIA, a novel peptide from the venom of *Conus tulipa* 1. Isolation, characterization and chemical synthesis. *Eur J Biochem.* **267**, 4642-4648.
73. Lewis RJ, Nielsen KJ, Craik DJ, Loughnan ML, Adams DA, Sharpe IA, Luchian T, Adams DJ, Bond T, Thomas L, Jones A, Matheson JL, Drinkwater R, Andrews PR, Alewood PF. (2000) Novel ω -conotoxins from *Conus catus* discriminate among neuronal calcium channel subtypes. *J. Biol. Chem.* **275**, 35335-35344.
74. Blanchfield, J., Dutton, J., Craik, D., Adams, D., Lewis, R., Alewood, P and Toth, I. (2001) The synthesis and structure of an N-terminal dodecanoic acid conjugate of α -conotoxin MII. *Lett Peptide Sci.* **8**, 235-239.
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76. Lewis R.J. (2001) The changing face of ciguatera. *Toxicon* **39**, 97-106.
77. Sharpe IA, Gehrmann J, Loughnan ML, Thomas L, Adams DA, Atkins A, Palant, E., Craik, DJ, Adams DF, Alewood PF, Lewis, RJ (2001) Two new classes of conopeptides inhibit the α_1 -adrenoceptor and noradrenaline transporter. *Nature Neurosci.* **4**, 902-907.
78. Hamilton, B., Mira Hurbungs, Jean-Paul Vernoux, Alun Jones and Richard J. Lewis (2002) Isolation and characterisation of Indian Ocean ciguatoxin. *Toxicon* **40**, 685-693.
79. Smith, M., P. J. Cabot, F. B. Ross, A. D. Robertson and R. J. Lewis (2002) The novel N-type

calcium channel blocker, AM336, produces potent dose-dependent antinociception after intrathecal dosing in rats and inhibits substance P release in rat spinal cord slices. *Pain* 96, 119-127.

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81. Nielsen K.J., Watson M., Adams D.J., Hammarström A.K., Gage P.W., Hill J.M., Craik D.J., Thomas L., Adams D., Alewood P.F., Lewis R.J. (2002) Solution structure of μ -conotoxin PIIIA, a preferential inhibitor of persistent TTX-sensitive sodium channels. *J. Biol. Chem.* 277, 27247-27255.
82. Hogg, R.C., Lewis, R.J., Adams D.J. (2002) Ciguatoxin-induced oscillations in membrane potential and action potential firing in rat parasympathetic neurons. *Eur. J. Neurosci.* 16, 242-248.
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92. Sharpe IA, Palant E, Schroeder CI, Kaye DM, Adams DJ, Alewood PF, Lewis RJ. (2003) Inhibition of the norepinephrine transporter by the venom peptide χ -MrIA: site of action, Na⁺ dependence, and structure-activity relationship. *J Biol Chem.* 278, 40317-40323.
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95. Loughnan M, Nicke A, Jones A, Adams DJ, Alewood PF and Lewis RJ (2003) Chemical and functional identification and characterization of novel sulfated α -conotoxins from the cone snail *Conus anemone*. *J. Med Chem.* (in press).
96. Pottier I, Hamilton B, Jones A, Lewis RJ and Vernoux J-P (2003) Identification of slow and fast-acting toxins in a highly ciguatoxic barracuda (*Sphyraena barracuda*) by HPLC/MS and radiolabelled ligand binding. *Toxicon* 42, 663-672.

Full published conference proceedings (most peer reviewed):

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Patents:

Inventor on three patents/applications covering the χ -conopeptides, one patent/application covering ω -conotoxins, one patent/application covering ρ -conopeptides, and one patent application covering μ -conotoxins.